```
=> d his

     (FILE 'HOME' ENTERED AT 09:21:05 ON 05 MAY 2008)

     FILE 'REGISTRY' ENTERED AT 09:21:39 ON 05 MAY 2008
                E MESNA/CN
L1             1 S E3

     FILE 'CAPLUS' ENTERED AT 09:22:54 ON 05 MAY 2008
L2           655 S L1
L3          3251 S END STAGE RENAL DISEASE
L4             2 S L2 AND L3

     FILE 'USPATFULL, USPATOLD, USPAT2' ENTERED AT 09:24:57 ON 05 MAY 2008
L5           205 S L1
L6          2455 S END STAGE RENAL DISEASE
L7             1 S L5 AND L6
                 SAVE TEMP ALL A10596479/L

     FILE 'MEDLINE, BIOSIS, EMBASE, WPIX, JAPIO, PASCAL, DISSABS' ENTERED AT
     09:31:59 ON 05 MAY 2008
L8          5212 S L1
L9          6820 S MESNA
L10         6882 S L8 OR L9
L11        44802 S END STAGE RENAL DISEASE
L12            8 S L10 AND L11
```

L12 ANSWER 1 OF 8 MEDLINE on STN
ACCESSION NUMBER: 2006745840 MEDLINE <<LOGINID::20080505>>
DOCUMENT NUMBER: PubMed ID: 17185151
TITLE: The effect of mesna on plasma total homocysteine concentration in hemodialysis patients.
AUTHOR: Urquhart Bradley L; Freeman David J; Spence J David; House Andrew A
CORPORATE SOURCE: Department of Medicine, University of Western Ontario, Canada.
SOURCE: American journal of kidney diseases : the official journal of the National Kidney Foundation, (2007 Jan) Vol. 49, No. 1, pp. 109-17.
Journal code: 8110075. E-ISSN: 1523-6838.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE) (RESEARCH SUPPORT, NON-U.S. GOV'T)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200702
ENTRY DATE: Entered STN: 23 Dec 2006
Last Updated on STN: 21 Feb 2007
Entered Medline: 20 Feb 2007
AB BACKGROUND: Plasma total homocysteine (tHcy) level is an independent risk factor for the development of atherosclerosis. The degree of risk in most of the population is decreased by using dietary vitamin supplementation; however, more than 90% of patients with end-stage renal disease have increased tHcy levels despite supplementation. Only a small fraction of tHcy is removed by hemodialysis because of extensive disulfide bonding to albumin. The objective of this study is to determine whether a single intravenous dose of mesna , a thiol-containing drug analogue of taurine, facilitates tHcy clearance during hemodialysis. METHODS: Initial in vitro thiol exchange tests were performed with mesna in plasma from dialysis patients. Mesna, 300 micromol/L (49.2 mg/L), was incubated with plasma at 37 degrees C, and free homocysteine was measured at various times. In vivo, mesna activity was tested in 10 hemodialysis patients by administering 2.5 or 5.0 mg/kg of mesna intravenously at the beginning of a treatment cycle. Blood samples were drawn throughout dialysis, and plasma tHcy levels were compared with those obtained from a previous dialysis session in which mesna was not administered. RESULTS: In vitro, mesna liberated 36.5% +/- 2.5% of protein-bound homocysteine in 30 minutes. In vivo, a single 2.5-mg/kg dose of mesna was ineffective; however, at 5.0 mg/kg, it caused a 55.2% +/- 3.9% decrease in plasma tHcy levels postdialysis compared with a 34.2% +/- 5.3% decrease with dialysis alone (P < 0.001). CONCLUSION: Intravenous mesna causes a rapid decrease in plasma tHcy levels during hemodialysis.

L12 ANSWER 2 OF 8 EMBASE
ACCESSION NUMBER: 2006627570 EMBASE <<LOGINID::20080505>>
TITLE: Clinical outcomes of childhood lupus nephritis: A single center's experience.
AUTHOR: Lee, Byong Sop; Cho, Hee Yeon; Kim, Eo Jin; Kang, Hee Gyung; Ha, Il Soo; Cheong, Hae Il; Kim, Joong Gon; Choi,

Yong (correspondence)
CORPORATE SOURCE: Department of Pediatrics, Seoul National University Children's Hospital, 28 Yongon-dong, Chongno-gu, Seoul 110-744, Korea, Republic of. ychoi@snu.ac.kr
AUTHOR: Lee, Hyun Soon
CORPORATE SOURCE: Department of Pathology, Seoul National University College of Medicine, Seoul, Korea, Republic of.
SOURCE: Pediatric Nephrology, (Feb 2007) Vol. 22, No. 2, pp. 222-231.
Refs: 55
ISSN: 0931-041X CODEN: PEDNEF
COUNTRY: Germany
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 028 Urology and Nephrology
037 Drug Literature Index
038 Adverse Reactions Titles
007 Pediatrics and Pediatric Surgery
LANGUAGE: English
SUMMARY LANGUAGE: English
ENTRY DATE: Entered STN: 30 Jan 2007
Last Updated on STN: 30 Jan 2007
AB This study retrospectively reviewed the medical records of children with lupus nephritis (LN) who were treated at Seoul National University Children's Hospital from 1986 to 2005 (mean duration 8.3±4.4 years). The records of 77 children (22 male and 55 female) were examined. The mean age at diagnosis was 11.9±3.0 years. The initial biopsy results revealed a WHO class IV classification for 60 (88.2%) of 68 biopsy proven cases. Of 77 patients, 67 (87.0%) responded initially to the high-dose corticosteroids with or without additional immunosuppressive therapy. Of the initial responders (67), 30 (44.8%) experienced at least one episode of proteinuric (24) or nephritic (6) flare. Thirteen patients (16.9%) progressed to either chronic renal failure (CRF) or end-stage renal disease (ESRD). Six (7.8%) patients died. A Kaplan-Meier estimate of patient survival and CRF-free survival rate was 95.4% and 88.7% at 5 years and 91.8% and 74.7% at 10 years, respectively. Multivariate analysis for class IV LN revealed male gender (P=0.029), initial hypertension (P=0.001) and absence of remission (P=0.002) to be prognostic factors predicting CRF. Glomerulosclerosis of 10% or more (P=0.005), nephritic flare (P=0.011), and presence of anti-phospholipid antibody (P=0.017) or syndrome (P=0.004) were also found to be independent risk factors for CRF. Cyclophosphamide pulse therapy failed to demonstrate superiority over other combined immunosuppressants used for the treatment of diffuse proliferative LN. .COPYRGT. IPNA 2006.

ACCESSION NUMBER: 2006614813 EMBASE <<LOGINID::20080505>>
TITLE: The Effect of Mesna on Plasma Total Homocysteine Concentration in Hemodialysis Patients.
AUTHOR: Urquhart, Bradley L.; Freeman, David J.; Spence, J. David; House, Andrew A., Dr. (correspondence)
CORPORATE SOURCE: Departments of Medicine and Physiology and Pharmacology, University of Western Ontario, Lawson Health Research Institute, London, Ont., Canada. andrew.house@lhsc.on.ca
SOURCE: American Journal of Kidney Diseases, (Jan 2007) Vol. 49, No. 1, pp. 109-117.

Refs: 46
ISSN: 0272-6386 CODEN: AJKDDP
PUBLISHER IDENT.: S 0272-6386(06)01511-3
COUNTRY: United States
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 018 Cardiovascular Diseases and Cardiovascular Surgery
028 Urology and Nephrology
037 Drug Literature Index
LANGUAGE: English
SUMMARY LANGUAGE: English
ENTRY DATE: Entered STN: 26 Jan 2007
Last Updated on STN: 26 Jan 2007

AB Background: Plasma total homocysteine (tHcy) level is an independent risk factor for the development of atherosclerosis. The degree of risk in most of the population is decreased by using dietary vitamin supplementation; however, more than 90% of patients with end-stage renal disease have increased tHcy levels despite supplementation. Only a small fraction of tHcy is removed by hemodialysis because of extensive disulfide bonding to albumin. The objective of this study is to determine whether a single intravenous dose of mesna , a thiol-containing drug analogue of taurine, facilitates tHcy clearance during hemodialysis. Methods: Initial in vitro thiol exchange tests were performed with mesna in plasma from dialysis patients. Mesna, 300 μmol/L (49.2 mg/L), was incubated with plasma at 37°C, and free homocysteine was measured at various times. In vivo, mesna activity was tested in 10 hemodialysis patients by administering 2.5 or 5.0 mg/kg of mesna intravenously at the beginning of a treatment cycle. Blood samples were drawn throughout dialysis, and plasma tHcy levels were compared with those obtained from a previous dialysis session in which mesna was not administered. Results: In vitro, mesna liberated 36.5% ± 2.5% of protein-bound homocysteine in 30 minutes. In vivo, a single 2.5-mg/kg dose of mesna was ineffective; however, at 5.0 mg/kg, it caused a 55.2% ± 3.9% decrease in plasma tHcy levels postdialysis compared with a 34.2% ± 5.3% decrease with dialysis alone ($P < 0.001$). Conclusion: Intravenous mesna causes a rapid decrease in plasma tHcy levels during hemodialysis. .COPYRGT. 2006 National Kidney Foundation, Inc.

ACCESSION NUMBER: 2006031560 EMBASE <<LOGINID::20080505>>

TITLE: Intravenous pulse cyclophosphamide therapy in focal segmental glomerulosclerosis.

AUTHOR: Buyukcelik, M., Dr. (correspondence); Dursun, H.; Soran, M.; Bayazit, A.K.; Noyan, A.; Anarat, A.
CORPORATE SOURCE: Department of Pediatric Nephrology, Cukurova University, School of Medicine Adana, Balcali, Adana 01330, Turkey. buyukcelikm66@yahoo.com
AUTHOR: Cengiz, N.
CORPORATE SOURCE: Department of Pediatric Nephrology, Baskent University, Medical Faculty, Adana, Turkey.
AUTHOR: Buyukcelik, M., Dr. (correspondence)
CORPORATE SOURCE: Department of Pediatrics Nephrology, Cukurova University School of Medicine, Balcali, Adana 01330, Turkey. buyukcelikm66@yahoo.com

SOURCE: Clinical Nephrology, (Jan 2006) Vol. 65, No. 1, pp. 7-12.
Refs: 25
ISSN: 0301-0430 CODEN: CLNHBI
COUNTRY: Germany
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 028 Urology and Nephrology
037 Drug Literature Index
038 Adverse Reactions Titles
007 Pediatrics and Pediatric Surgery
LANGUAGE: English
SUMMARY LANGUAGE: English
ENTRY DATE: Entered STN: 24 Feb 2006
Last Updated on STN: 3 Mar 2006

AB Aims: We herein report the results of intravenous pulse cyclophosphamide (IVCP) therapy of 5 patients with steroid-resistant focal segmental glomerulosclerosis (FSGS). All patients had been treated with oral and intravenous pulse methylprednisolone and failed to respond to steroids from onset and were considered as primary steroid-resistant. Before starting IVCP, all patients were also treated with other immunosuppressive drugs with or without steroids, but none of them responded to such therapies and no patient had any NPSH2 gene mutations. Methods: IVCP was given monthly at a dose of 500 mg/m(2) for 6 months. At the end of 6 months, IVCP was discontinued in case there was no response. Otherwise, IVCP was continued for every 2 months. Oral prednisone was given concurrently at 60 mg/m(2) daily for 6 weeks and then 40 mg/m(2) on alternate days for 4 weeks. Prednisone was then tapered to 10 mg/m(2) alternate days and continued during the therapy period. Results: Only 1 of these patients achieved remission after IVCP while 4 patients showed no response to IVCP. 2 patients who did not achieve remission progressed to end-stage renal disease (ESRD) and 2
others who had not been treated with cyclosporine before underwent cyclosporine therapy. None of our patients has suffered from adverse effects of IVCP. Conclusion: We found that IVCP had a limited beneficial effect in treatment of steroid-resistant FSGS and it may be suggested that IVCP can be tried to treat steroid-resistant patients, also for patients with primary steroid resistance and those who do not respond to other immunosuppressive therapies. .COPYRGT. 2006 Dustri-Verlag Dr. K. Feistle.

L12 ANSWER 5 OF 8 EMBASE

ACCESSION NUMBER: 2004071114 EMBASE <<LOGINID::20080505>>
TITLE: Pulse cyclophosphamide therapy for steroid-resistant focal segmental glomerulosclerosis in children.
AUTHOR: Al Salloum, Abdullah A., Dr. (correspondence)
CORPORATE SOURCE: Department of Pediatrics, College of Medicine, King Khalid University Hospital, P.O. Box 2925, Riyadh 11461, Saudi Arabia. asol333@hotmail.com
AUTHOR: Al Salloum, Abdullah A., Dr. (correspondence)
CORPORATE SOURCE: Department of Pediatrics 39, College of Medicine, KKUH/King Saud University, P.O. Box 2925, Riyadh 11461, Saudi Arabia. asol333@hotmail.com
SOURCE: Annals of Saudi Medicine, (Jan 2004) Vol. 24, No. 1, pp. 27-30.
Refs: 16
ISSN: 0256-4947 CODEN: ANSMEJ

COUNTRY: Saudi Arabia
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 028 Urology and Nephrology
037 Drug Literature Index
038 Adverse Reactions Titles
007 Pediatrics and Pediatric Surgery
LANGUAGE: English
SUMMARY LANGUAGE: English
ENTRY DATE: Entered STN: 26 Feb 2004
Last Updated on STN: 1 Feb 2007

AB Background: In children, steroid-resistant nephritic syndrome due to focal segmental glomerulosclerosis (FSGS) is frequently a progressive condition resulting in end-stage renal disease (ESRD). We report the response of 15 patents with steroid resistant FSGS to treatment with intravenous pulse cyclophosphamide (IVCP) and oral prednisone after 4 years of follow up. Five patients had initial steroid resistance and ten patients had late steroid resistance. Patients and Methods: All patients were treated with IVCP at a dose of 500 mg/m(2)/month for 6 months. Adjunctive prednisolone was given at a dose of 60 mg/m(2)/day for 4 weeks followed by 40 mg/m(2)/ on alternate days for 4 weeks and then tapered over next 4 weeks. Results: All patients with initial resistance to steroids showed no response to IVCP and continued to be steroid resistant. Three developed CRF during the observation period. The other ten patients with late steroid resistance responded to IVCP, but all were steroid dependent at the end of the observation period. Five could not be weaned from steroids during the IVCP treatment period. The other five patients achieved relatively prolonged remission (7 months to 24 months), but eventually become steroid dependent. Conclusion: Sixty-seven percent of steroid-resistant FSGS becomes steroid dependent. Patients with initial steroid resistance did not respond to IVCP. We found no correlation between IgM deposition and the response to therapy. The side effects of IVCP were negligible. Beneficial therapy for initial steroid-resistant FSGS remains to be determined.

L12 ANSWER 6 OF 8 WPIX COPYRIGHT 2008 THE THOMSON CORP on STN
ACCESSION NUMBER: 2005-479208 [48] WPIX
DOC. NO. CPI: C2005-145861 [48]
TITLE: Use of sodium 2-mercaptoethylsulfonate for treating elevated plasma total homocysteine levels in subjects with end stage renal disease
DERWENT CLASS: B05
INVENTOR: FREEMAN D; FREEMAN D J; HOUSE A; HOUSE A A; SPENCE J; SPENCE J D; URQUHART B; URQUHART B L; SPENCE D J
PATENT ASSIGNEE: (LONH-N) LONDON HEALTH SCI CENT RES INC; (LONH-N) LONDON HEALTH SCI RES CENT INC; (FREE-I) FREEMAN D J; (HOUS-I) HOUSE A A; (SPEN-I) SPENCE D J; (URQU-I) URQUHART B L
COUNTRY COUNT: 107

PATENT INFO ABBR.:

PATENT NO	KIND	DATE	WEEK	LA	PG	MAIN IPC
WO 2005058300	A1	20050630	(200548)*	EN	48[16]	
EP 1701717	A1	20060920	(200662)	EN		

US 20070249729 A1 20071025 (200771) EN

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 2005058300	A1	WO 2004-CA2158	20041220
EP 1701717	A1	EP 2004-802333	20041220
EP 1701717	A1	WO 2004-CA2158	20041220
US 20070249729	A1 Provisional	US 2003-530237P	20031218
US 20070249729	A1	WO 2004-CA2158	20041220
US 20070249729	A1	US 2007-596479	20070329

FILING DETAILS:

PATENT NO	KIND		PATENT NO	
EP 1701717	A1	Based on	WO 2005058300	A

PRIORITY APPLN. INFO: US 2003-530237P 20031218
US 2007-596479 20070329

AN 2005-479208 [48] WPIX

AB WO 2005058300 A1 UPAB: 20051223

NOVELTY - A method (M1) of lowering elevated plasma total homocysteine (tHcy) levels in a subject with end stage renal disease (ESRD) involves administering sodium 2-mercaptoethylsulfonate (Mesna) or its derivative (diMesna).

ACTIVITY - Cardiant; Cerebroprotective; Vasotropic; Anticoagulant; Thrombolytic; Antiarteriosclerotic.

To evaluate in vivo effects of Mesna on plasma tHcy, 5 maintenance hemodialysis patients were recruited to participate in a single dose pilot study. Blood samples were drawn at selected intervals during a mid-week dialysis session during which no Mesna was given. One week later, subjects received a single, 5 mg/kg, pre-dialysis, intravenous dose of Mesna and blood samples were drawn throughout the dialysis session. Dialysate samples were also collected from patients. Total Hcy and cysteine were measured in plasma and dialysate by the modified method of Jacobsen et al. Mesna caused a profound, rapid decrease in plasma tHcy and cysteine. There was a slight increase in dialysate Hcy with Mesna treatment compared to control. Post-dialysis, plasma tHcy and cysteine were significantly decreased with Mesna compared to control. A pre-dialysis plasma sample was also drawn before the next dialysis session 2 days later. Plasma tHcy was 2.3 microns lower with Mesna than control indicating a residual effect of Mesna on tHcy concentrations.

MECHANISM OF ACTION - None given.

USE - For lowering elevated plasma total homocysteine (tHcy) levels in a subject (preferably human) with end stage renal disease and with risk of cardiovascular-related diseases e.g. myocardial infarction, stroke, thrombosis (e.g. venous thrombosis, dialysis access thrombosis and thrombotic stroke) and atherosclerosis (claimed).

ADVANTAGE - Intravenous Mesna causes a rapid decrease of total plasma homocysteine (tHcy) within 30 minutes of its administration to human subjects. Mesna resulted in a decrease of post-dialysis tHcy from 18 micronsol/L to 10.1 micronsol/L. A large portion of the

administered Mesna remained in plasma after the maximal Hcy effect occurred suggesting that a smaller dose could be used chronically when attempting to normalize plasma tHcy. Mesna was shown to be removed from plasma by dialysis and appeared in dialysis collected at various times throughout dialysis. Chronic, low dose Mesna administration represents a novel treatment option for ESRD associated hyperhomocysteinemia.

L12 ANSWER 7 OF 8 PASCAL COPYRIGHT 2008 INIST-CNRS. ALL RIGHTS RESERVED. on STN

ACCESSION NUMBER: 2007-0295690 PASCAL <<LOGINID::20080505>>
COPYRIGHT NOTICE: Copyright .COPYRGT. 2007 INIST-CNRS. All rights reserved.
TITLE (IN ENGLISH): The effect of mesna on Plasma total homocysteine concentration in hemodialysis patients
AUTHOR: URQUHART Bradley L.; FREEMAN David J.; SPENCE J. David; HOUSE Andrew A.
CORPORATE SOURCE: Departments of Medicine and Physiology and Pharmacology, University of Western Ontario, Canada; Lawson Health Research Institute; and Robarts Research Institute, London, Ontario, Canada
SOURCE: American journal of kidney diseases, (2007), 49(1), 109-117, 46 refs.
ISSN: 0272-6386
DOCUMENT TYPE: Journal
BIBLIOGRAPHIC LEVEL: Analytic
COUNTRY: United States
LANGUAGE: English
AVAILABILITY: INIST-19098, 354000149886960110
AN 2007-0295690 PASCAL <<LOGINID::20080505>>
CP Copyright .COPYRGT. 2007 INIST-CNRS. All rights reserved.
AB Background: Plasma total homocysteine (tHcy) level is an independent risk factor for the development of atherosclerosis. The degree of risk in most of the population is decreased by using dietary vitamin supplementation; however, more than 90% of patients with end-stage renal disease have increased tHcy levels despite supplementation. Only a small fraction of tHcy is removed by hemodialysis because of extensive disulfide bonding to albumin. The objective of this study is to determine whether a single intravenous dose of mesna , a thiol-containing drug analogue of taurine, facilitates tHcy clearance during hemodialysis. Methods: Initial in vitro thiol exchange tests were performed with mesna in plasma from dialysis patients. Mesna, 300 μmol/L (49.2 mg/L), was incubated with plasma at 37°C, and free homocysteine was measured at various times. In vivo, mesna activity was tested in 10 hemodialysis patients by administering 2.5 or 5.0 mg/kg of mesna intravenously at the beginning of a treatment cycle. Blood samples were drawn throughout dialysis, and plasma tHcy levels were compared with those obtained from a previous dialysis session in which mesna was not administered. Results: In vitro, mesna liberated 36.5% ± 2.5% of protein-bound homocysteine in 30 minutes. In vivo, a single 2.5-mg/kg dose of mesna was ineffective; however, at 5.0 mg/kg, it caused a 55.2% ± 3.9% decrease in plasma tHcy levels postdialysis compared with a 34.2% ± 5.3% decrease with dialysis alone ($P < 0.001$). Conclusion: Intravenous mesna causes a rapid decrease in plasma tHcy levels during hemodialysis.

L12 ANSWER 8 OF 8 DISSABS COPYRIGHT (C) 2008 ProQuest Information and Learning Company; All Rights Reserved on STN

ACCESSION NUMBER: 2008:19454 DISSABS Order Number: AAINR30758
TITLE: Evaluation of hyperhomocysteinemia in patients with end-stage renal disease
AUTHOR: Urquhart, Bradley L. [Ph.D.]
CORPORATE SOURCE: The University of Western Ontario (Canada) (0784)
SOURCE: Dissertation Abstracts International, (2006) Vol. 68, No. 9B, p. 5882. Order No.: AAINR30758. 238 pages.
ISBN: 978-0-494-30758-8.
DOCUMENT TYPE: Dissertation
FILE SEGMENT: DAI
LANGUAGE: English
ENTRY DATE: Entered STN: 20080328
Last Updated on STN: 20080328

AB Homocysteine (Hey) is a thiol-containing amino acid derived as a by-product of essential transmethylation reactions. Hey lies at a key junction of the methylation cycle where it may be salvaged to methionine or irreversibly catabolized to cysteine. Elevated plasma total homocysteine (tHcy) is a graded, independent risk factor for atherosclerosis and heart disease. Plasma tHcy is effectively normalized by vitamin supplementation however; patients with end-stage renal disease (ESRD) are resistant to this treatment. Patients with ESRD are especially interesting because (1) over 85% have elevated plasma tHcy, (2) the leading cause of morbidity and mortality are due to cardiovascular disease, (3) the cause of hyperhomocysteinemia is unknown and (4) there are no treatments to normalize tHcy in this population.

We evaluated the export of Hey from uremic erythrocytes; a non-invasive model of the balance between Hey synthesis and remethylation to clarify the cause of ESRD associated hyperhomocysteinemia. Opposite to our hypothesis Hey export was significantly decreased from uremic erythrocytes when compared to those from healthy controls. These results demonstrate decreased transmethylation in patients with ESRD and point to impaired clearance of Hey by transsulfuration as the cause of ESRD associated hyperhomocysteinemia.

Recent investigations to lower tHcy in patients with ESRD have focused on administration of thiol-compounds to exchange Hey from protein and increase its clearance. As these trials have had variable success, we developed an in vitro assay that predicts the efficacy of thiol compounds to exchange with protein bound Hey prior to performing expensive trials. We then screened several thiol compounds to discover new treatments for ESRD associated hyperhomocysteinemia. Mesna, a thiol agent used to prevent ifosfamide-induced hemorrhagic cystitis, was highly effective in our in vitro assay. When evaluated in single-dose pilot studies, intravenous and oral mesna caused significant decreases in plasma tHcy in patients with ESRD and healthy controls, respectively. However; a preliminary randomized controlled-trial of intravenous mesna in hemodialysis patients failed to show a sustained decrease in plasma tHcy suggesting higher doses are required to lower tHcy by a clinically relevant degree.

KEYWORDS: Homocysteine; End-Stage Renal Disease; Hemodialysis; Thiol Exchange; Atherosclerosis; Mesna.

L7 ANSWER 1 OF 1 USPATFULL on STN
ACCESSION NUMBER: 2007:285173 USPATFULL <<LOGINID::20080505>>
TITLE: Method of Treating Elevated Plasma Homocysteine Levels in Esrd Patients
INVENTOR(S): Urquhart, Bradley L., Thornhill, CANADA
Freeman, David J., London, CANADA
House, Andrew A., London, CANADA
Spence, David J., London, CANADA

	NUMBER	KIND	DATE	
PATENT INFORMATION:	US 2007249729	A1	20071025	
APPLICATION INFO.:	US 2004-596479	A1	20041220	(10)
	WO 2004-CA2158		20041220	
			20070329	PCT 371 date

	NUMBER	DATE
PRIORITY INFORMATION:	US 2003-530237P	20031218 (60)

DOCUMENT TYPE: Utility
FILE SEGMENT: APPLICATION
LEGAL REPRESENTATIVE: BERESKIN AND PARR, 40 KING STREET WEST, BOX 401, TORONTO, ON, M5H 3Y2, CA
NUMBER OF CLAIMS: 16
EXEMPLARY CLAIM: 1
NUMBER OF DRAWINGS: 16 Drawing Page(s)
LINE COUNT: 863
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L4 ANSWER 1 OF 2 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2007:150029 CAPLUS <<LOGINID::20080505>>
DOCUMENT NUMBER: 146:308324
TITLE: The effect of mesna on plasma total homocysteine concentration in hemodialysis patients
AUTHOR(S): Urquhart, Bradley L.; Freeman, David J.; Spence, J. David; House, Andrew A.
CORPORATE SOURCE: Departments of Medicine and Physiology and Pharmacology, University of Western Ontario, London, ON, Can.
SOURCE: American Journal of Kidney Diseases (2006), Volume Date 2007, 49(1), 109-117
CODEN: AJKDDP; ISSN: 0272-6386
PUBLISHER: Elsevier
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Plasma total homocysteine (tHcy) level is an independent risk factor for the development of atherosclerosis. The degree of risk in most of the population is decreased by using dietary vitamin supplementation; however, more than 90% of patients with end-stage renal disease have increased they levels despite supplementation. Only a small fraction of tHcy is removed by hemodialysis because of extensive disulfide bonding to albumin. The objective of this study is to determine whether a single i.v. dose of mesna, a thiol-containing drug analog of taurine, facilitates tHcy clearance during hemodialysis. Initial in vitro thiol exchange tests were performed with mesna in plasma from dialysis patients. Mesna, 300 μmol/L (49.2 mg/L), was incubated with plasma at 37°C, and free homocysteine was measured at various times. In vivo, mesna activity was tested in 10 hemodialysis patients by administering 2.5 or 5.0 mg/kg of mesna i.v. at the beginning of a treatment cycle. Blood samples were drawn throughout dialysis, and plasma tHcy levels were compared with those obtained from a previous dialysis session in which mesna was not administered. In vitro, mesna liberated 36.5% ± 2.5% of protein-bound homocysteine in 30 min. In vivo, a single 2.5-mg/kg dose of mesna was ineffective; however, at 5.0 mg/kg, it caused a 55.2% ± 3.9% decrease in plasma tHcy levels postdialysis compared with a 34.2% ± 5.3% decrease with dialysis alone ($P < 0.001$). I.v. mesna causes a rapid decrease in plasma tHcy levels during hemodialysis.
REFERENCE COUNT: 46 THERE ARE 46 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT
AB . . . risk in most of the population is decreased by using dietary vitamin supplementation; however, more than 90% of patients with end-stage renal disease have increased they levels despite supplementation. Only a small fraction of tHcy is removed by hemodialysis because of extensive disulfide. . .
IT 19767-45-4, Mesna
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(effect of single i.v. dose of mesna on plasma total homocysteine concentration in hemodialysis patients)

L4 ANSWER 2 OF 2 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2005:570802 CAPLUS <<LOGINID::20080505>>
DOCUMENT NUMBER: 143:71775

TITLE: Method of treating elevated plasma homocysteine levels in end stage renal disease (ESRD) patients
INVENTOR(S): Urquhart, Bradley L.; Freeman, David J.; House, Andrew A.; Spence, J. David
PATENT ASSIGNEE(S): London Health Sciences Centre Research Inc., Can.
SOURCE: PCT Int. Appl., 48 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2005058300	A1	20050630	WO 2004-CA2158	20041220
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
CA 2582611	A1	20050630	CA 2004-2582611	20041220
EP 1701717	A1	20060920	EP 2004-802333	20041220
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, FI, RO, CY, TR, BG, CZ, EE, HU, PL, SK, IS				
US 20070249729	A1	20071025	US 2007-596479	20070329
PRIORITY APPLN. INFO.:			US 2003-530237P P	20031218
			WO 2004-CA2158 W	20041220

AB A method of treating elevated plasma total homocysteine levels (tHc) in subjects with end stage renal disease (ESRD) is disclosed, said treatment comprising the administration of sodium 2-mercaptoethylsulfonate (MESNA) immediately prior to, or concurrently with, performing hemodialysis on said patient.

REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

TI Method of treating elevated plasma homocysteine levels in end stage renal disease (ESRD) patients

AB A method of treating elevated plasma total homocysteine levels (tHc) in subjects with end stage renal disease (ESRD) is disclosed, said treatment comprising the administration of sodium 2-mercaptoethylsulfonate (MESNA) immediately prior to, or concurrently with, performing hemodialysis. . .

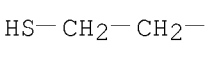
ST mercaptoethylsulfonate MESNA renoprotectant blood homocysteine end stage renal disease

IT Kidney, disease
(failure, chronic; method of treating elevated plasma homocysteine levels in end stage renal disease (ESRD) patients)

IT Dialysis
(hemodialysis; method of treating elevated plasma homocysteine levels

in end stage renal disease
(ESRD) patients)
IT Heart, disease
(infarction; method of treating elevated plasma homocysteine levels in end stage renal disease (ESRD)
patients)
IT Drug delivery systems
(injections, i.v.; method of treating elevated plasma homocysteine levels in end stage renal disease
(ESRD) patients)
IT Atherosclerosis
Cardiovascular system, disease
Combination chemotherapy
Human
Thrombosis
(method of treating elevated plasma homocysteine levels in end stage renal disease (ESRD) patients)
IT Drug delivery systems
(oral; method of treating elevated plasma homocysteine levels in end stage renal disease (ESRD)
patients)
IT Cytoprotective agents
(renoprotective agents; method of treating elevated plasma homocysteine levels in end stage renal disease
(ESRD) patients)
IT Brain, disease
(stroke; method of treating elevated plasma homocysteine levels in end stage renal disease (ESRD)
patients)
IT Thrombosis
(venous; method of treating elevated plasma homocysteine levels in end stage renal disease (ESRD)
patients)
IT 19767-45-4, MESNA
RL: ADV (Adverse effect, including toxicity); PAC (Pharmacological activity); PKT (Pharmacokinetics); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(method of treating elevated plasma homocysteine levels in end stage renal disease (ESRD) patients)
IT 52-90-4, Cysteine, biological studies 6027-13-0, L-Homocysteine
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(method of treating elevated plasma homocysteine levels in end stage renal disease (ESRD) patients)
IT 59-30-3, Folic acid, biological studies 12001-76-2, Vitamin B
16208-51-8, Di mesna 19767-45-4D, MESNA, derivative
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(method of treating elevated plasma homocysteine levels in end stage renal disease (ESRD) patients)

L1 ANSWER 1 OF 1 REGISTRY COPYRIGHT 2008 ACS on STN
RN 19767-45-4 REGISTRY
ED Entered STN: 16 Nov 1984
CN Ethanesulfonic acid, 2-mercapto-, sodium salt (1:1) (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN Ethanesulfonic acid, 2-mercapto-, monosodium salt (8CI, 9CI)
OTHER NAMES:
CN 2-Mercapto-1-ethanesulfonic acid monosodium salt
CN 2-Mercaptoethanesulfonic acid monosodium salt
CN 2-Mercaptoethanesulfonic acid sodium salt
CN D 7093
CN Mesna
CN Mesnex
CN Mesnum
CN Mistabron
CN Mistabronco
CN Mitexan
CN Mucofluid
CN Prehepon
CN Sodium 2-mercaptoethanesulfonate
CN UCB 3983
CN Uromitexan
DR 122504-78-3
MF C2 H6 O3 S2 . Na
CI COM
LC STN Files: ADISINSIGHT, ADISNEWS, AGRICOLA, ANABSTR, BEILSTEIN*, BIOSIS, BIOTECHNO, CA, CAPLUS, CASREACT, CBNB, CHEMCATS, CHEMINFORMRX, CHEMLIST, CIN, CSCHEM, DDFU, DRUGU, EMBASE, IFICDB, IFIPAT, IFIUDB, IMSCOSEARCH, IPA, MEDLINE, MRCK*, MSDS-OHS, PIRA, PROMT, PS, RTECS*, SYNTHLINE, TOXCENTER, USAN, USPAT2, USPATFULL, USPATOLD
(*File contains numerically searchable property data)
Other Sources: EINECS**, WHO
(**Enter CHEMLIST File for up-to-date regulatory information)
CRN (3375-50-6)



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

655 REFERENCES IN FILE CA (1907 TO DATE)
14 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
655 REFERENCES IN FILE CAPLUS (1907 TO DATE)